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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
| 10/568,215 | 03/28/2006 | Mary Lopez | NEN-22502/16 | 8128 |
| 37742 | 7590 | 03/24/2009 | EXAMINER | |
| GIFFORD, KRASS, SPRINKLE, ANDERSON & CITKOWSKI, P.C. P.O. BOX 7021 TROY, MI 48007-7021 | | | SHEN, BIN | |
| ART UNIT | PAPER NUMBER | | | |
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

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|------------------------------|--------------------------------------|------------------------------------|
| Office Action Summary | Application No. 10/568,215 | Applicant(s) LOPEZ, MARY |
| | Examiner BIN SHEN | Art Unit 1657 |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
 - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
 - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED. (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 29 December 2008.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-19,21,22,24-28 and 30-34 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1-19,21,22,24-28 and 30-34 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) Notice of References Cited (PTO-892)
 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
 3) Information Disclosure Statement(s) (PTO/SB/08)
 Paper No(s)/Mail Date _____
- 4) Interview Summary (PTO-413)
 Paper No(s)/Mail Date _____
- 5) Notice of Informal Patent Application
 6) Other: _____

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 29 December 2008 has been entered.

Status of the Claims

Claims 1-19, 21, 22, 24-28 and 30-34 are considered on the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-12, 14-19, 21, 22, 24-25, 27-28, 30-32, 34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 15 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. Claims 1 and 15 are incomplete because they lack analyzing step to accomplish the preamble of the claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

- (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-12, 14-19, 21, 22, 24-25, 27-28, 30-32, 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Wagner et al. in view of each of Gygi et al. (PNAS 2000 97(17):9390-9395) and Kachman et al. (Anal. Chem. 2002 74:1779-1791).

Wagner teaches a process for analyzing proteins in a sample comprising dividing a sample into plurality of aliquots (page 810, right column, 5th and 6th full paragraph); applying to a first separation step to yield a plurality of partially resolved eluates; subjecting said plurality of partially resolved eluates to a second separation step; collecting at least one of said plurality of resolved fractions (page 811, left column, 1st-3rd full paragraph); analyzing the resolved fractions by mass spectrometry (page 813, left column, 1st full paragraph); wherein collection of the at least one of said plurality of resolved fractions occurs onto a MALDI target (page 813, left column, 1st full paragraph); wherein the separation steps separate on a basis selected from the group consisting of: charge, molecular weight, and hydrophobicity and using chromatography resin, and the separation buffer varies monotonically between individual aliquots, and the separation steps comprises a separation matrix in linear (page 811, left column, 1st-3rd full paragraph, and page 812, Fig. 1) or two-dimensional array (page 811, right column, under 2D-HPLC system).

Wagner does not teach that the mass spectrometry is performed on an orthogonal MALDI mass spectrometer, digesting a plurality of partially resolved eluates with a proteolytic enzyme to yield a plurality of digested eluates, labeling a sample with tagged or machine-readable labels, applying a plurality of aliquots in parallel to first separation step by a robot. However, Wagner suggests the automation of the process using robotic equipment (page 820, right column, 1st full paragraph, line 7).

Gygi teaches a method of protein analysis comprising tryptic digestion of samples before separated by chromatography (page 9393, right column, 1st full paragraph, line 8) in mass spectrometry for protein identification (abstract), and suggests to develop novel techniques that permit large-scale (automation) quantitative comparison of protein expression (page 9395, right column, end of Conclusions).

Kachman teaches a method of protein analysis by tagging protein in fraction in mass mapping method for interlysate comparison of protein expression (abstract, line 14, also see page 1786, left column, lines 16-18), and its potential to be automated (page 1791, right column, line 2).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Wagner by digesting and tagging protein samples in each fraction to analyze protein with MALDI mass spectrometer because Wagner teaches that multidimensional separation can be performed on digested protein (page 810, right column, 1st full paragraph) and Gygi teaches a digestion step in the mass spectrometer protein analysis. One would have been motivated to make the modification and automate the process using a robotic equipment because Wagner et al. specifically described the benefits of on-line array fractionation onto targets for MALDI-TOFMS (page 820, right column, 1st full paragraph), and would reasonably have expected success in view of Kachman's teaching of a protein tagging method for accurate mass analysis (page 1786, left column, lines 16-18) and its potential for automation.

A person of ordinary skill in the art, upon reading the references, would also have recognized the desirability to improve the method by performing the separation process multiple times either simultaneously as in parallel processing or sequentially for the obvious time saving by automation with predictable success because a person of ordinary skill has good reason to pursue the known options within his/her technical grasp.

Claims 1-6, 8-11, 13, 26, 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Wagner et al. in view of Miliotis et al. (2000).

Wagner teaches what is above.

Wagner does not teach that the separation steps occurs within a microplate with matrices maintaining well addresses in each of the two matrices, the collection (fractions/eluates affixing a machine-readable label.

Miliotis teach a process for analyzing proteins where the chromatographic separation is continuously transferred onto a plate as discrete spots (fractions/eluates) in a precise array pattern (abstract, lines 5-6).

A person of ordinary skill in the art at the time the invention was made would have been motivated to develop an integrated protein identification platform using microplate to substitute for the MALDI target plate and collect fraction/eluates in a precise array pattern because Miliotis teach the transferring of the separation fraction onto a MALDI target plate in an array (abstract; Fig 1).

Hence, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to affixing a machine-readable label to the fraction/eluates collection to simplify automation and increase the robustness of the system (see motivation for this improvement on page 109, end of the left column).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments filed 12/29/2008 have been fully considered but they are not persuasive.

Applicant argues that Wagner fails to teach or suggest all elements of the claim (does not teach applying said plurality of aliquots in parallel to a first separation step).

It is the examiner's position that Wagner teach dividing a sample into a plurality of aliquots (page 810, right column, end of 5th full paragraph, "A 2-ml portion of the sample...", and beginning of 6th full paragraph, "A 3-ml portions of ..."), thus sample were divided into plurality of aliquots, even though they were not applying in parallel to separation steps. However, it is the examiner's position that the first step of claim 1 (dividing a sample into a plurality of aliquots) is patentably indistinguishable (only changes the size of the sample) from Wagner's teaching and does not change the result of the process, thus a person of ordinary skill in the art after reading the cited references for the purpose of saving time/automation (as taught by Kachman on page 1791, right column, line 2) would improve the method by performing the

separating steps multiple times either in parallel or sequentially for the anticipated success as taught by Wagner.

Conclusion

No claim is allowed.

Certain papers related to this application may be submitted to Art Unit 1657 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone number for the Group is 571-273-8300. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-

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9199.

Any inquiry concerning rejections or objections in this communication or earlier communications from the examiner should be directed to Bin Shen, whose telephone number is (571) 272-9040. The examiner can normally be reached on Monday through Friday, from about 9:00 AM to about 5:30 PM. A phone message left at this number will be responded to as soon as possible (i.e., shortly after the examiner returns to her office).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached at (571) 272-0925.

B Shen

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/JON P WEBER/
Supervisory Patent Examiner, Art Unit 1657